Composition Imaging System for Intravascular Optical Coherence Tomography "Compovision-OCT"

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We have developed an optical coherence tomography system, Compovision-OCT (CV-OCT) that detects lipid for intravascular diagnosis. This system is developed by combining our proprietary Compovision technology, which visualizes the composition of the object using near-infrared light, and optical coherence tomography, which visualizes the cross-sectional tomographic image of the object using interference of light. The main feature of CV-OCT is that it utilizes the near-infrared light in the 1.7 μm wavelength band, which shows an absorption peak of lipid contained in coronary artery plaque. To achieve a performance needed in clinical applications, this system employs a broadband light source based on super-luminescent diodes and spectroscopic line camera. This results in an acquisition rate of 47 kHz per a line of cross-sectional image, and a sensitivity over 100 dB for detecting weak light reflected from the object. We also demonstrate lipid distribution imaging by CV-OCT using an artificial coronary artery plaque model, and confirm the accuracy for lipid detection is more than 90%, which would be sufficiently high for application to plaque diagnosis. This paper presents the feature, configuration, image processing, basic performance of the CV-OCT system and results of evaluation using coronary plaque model.

Keywords: optical coherence tomography, intravascular diagnostics, plaque, Compovision, super-luminescent diode

1. Introduction

Now that we are facing the advent of the super-aging society where people over 65 years old account for greater than a quarter of the nation's population, the growth of medical spending is becoming a serious social problem. Under these circumstances, efficient treatment that accords with the seriousness of the disease is required to reduce medical spending, and diagnostic methods to obtain more detailed information are needed.

In the meantime, heart disease ranks second in causes of death in Japan, and as ischemic heart disease due to coronary arteriosclerosis with approximately 80% of the deaths[1] can lead to acute symptoms, it is crucial to detect it on the early stage. Intravascular imaging diagnostics using a coronary catheter[*1] is one of the methods used to diagnose the condition of the coronary arteries in detail. While intravascular ultrasonic echo have been mainly used optical coherence tomography (OCT) is currently attracting attention as an optical one.

OCT, featuring extremely high resolutions of 10 to 15 μm in the depth direction, allows doctors to accurately grasp the state of the stent placed in the artery for treatment, and to detect vulnerable plaque[*2] that is considered to cause acute heart diseases[2]. OCTs have already been introduced in intravascular diagnostic systems, and reimbursement of medical expenses in OCT started in October 2008.

In ordinary OCT, images are obtained using the strength of scattered light within the target, and composition information for the target cannot be directly acquired. On the other hand, intravascular plaque is classified by its composition into several types each of which requires different treatment. Doctors thus have to make judgments based on empirical rules even when diagnosing using intravascular OCT, and the reliability of the diagnosis depends on the proficiency of the doctor. We consider that the stability of plaque can be precisely determined regardless of the proficiency of the doctor if there is any method that directly determines the plaque composition with intravascular OCT, thus contributing to qualitative progress in diagnosis.

Our company has already developed an analysis system, Compovision[*3] [3], which visualizes the composition distribution of the target using near-infrared lights and we have now come up with an intravascular OCT system, Compovision OCT (CV-OCT), which detects the composition distribution by applying the technique used in Compovision to intravascular OCT[4, 5]. This article introduces the characteristics, structure, image processing and performance of our CV-OCT system and reports the demonstration results using a vascular plaque model.

2. Principle of OCT

Figure 1 shows the concept of OCT. CV-OCT is based on Fourier-domain OCT (FD-OCT)[*4], which generates images with Fourier analysis[*5] from the wavelength spectrum of the interfering light obtained with a light source having a broad wavelength spectrum and a spectroscopic line camera to detect the spectrum.

OCT divides the light beam emitted by a light source into two optical paths and irradiates the light beam passing through one of the optical paths (measurement light) onto the measurement target. Then, the minute amount of light returned from the scattered light is combined with the light beam passing through the other optical path (reference light), and the spectroscopic line camera detects the interference spectrum caused by the optical path length

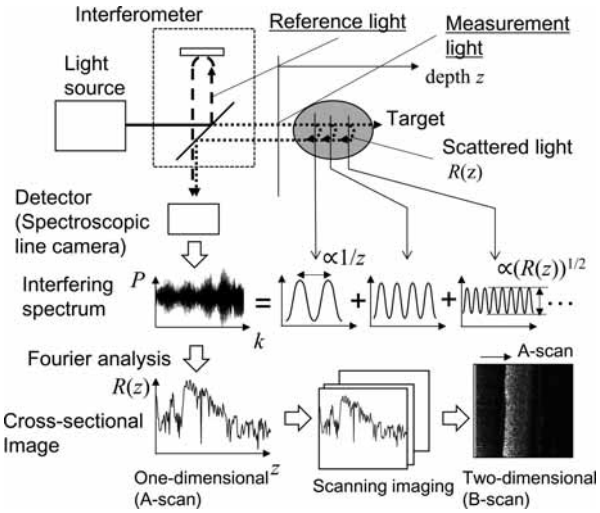

Fig. 1. Concept of OCT (Fourier-Domain OCT)

difference. Assuming an interference spectrum obtained by light scattering at a particular point, the amplitude is proportional to the square root of the scattering rate, and the period is inversely proportional to the depth from the optical path length difference. As the thus obtained interference spectrum appears superposed on the interference spectrum obtained through scattering at each point, the distribution of scattering intensities against depth can be obtained via Fourier analysis as a one-dimensional cross-sectional image (A-scan image). In addition, A-scan images obtained by scanning the measurement light in a vertical direction to the depth are combined to obtain a two-dimensional cross-sectional image (B-scan image).

3. Compovision OCT (CV-OCT)

3-1 Characteristics of CV-OCT

While conventional intravascular OCTs employ light with a wavelength of 1.3 μm that has low absorption by water, CV-OCT uses light at a wavelength of 1.7 μm. When the absorption spectra of water, vessel, and the lipid that comprises the plaque are compared within a range from 1.3 μm to 1.7 μm (**Fig. 2**), no difference is observed in the spectral shapes between the vessel and the lipid at 1.3 μm, but the lipid shows an absorption peak due to C-H bonds at 1.7 μm. Thus lipid can be quantitatively detected by extracting the difference in the absorbed quantity between the wavelengths from the interference spectra in the band around 1.7 μm. As the lipid can be visualized in the depth-direction distribution as in ordinary OCT, the state of the plaque can be grasped more accurately than with conventional intravascular OCT.

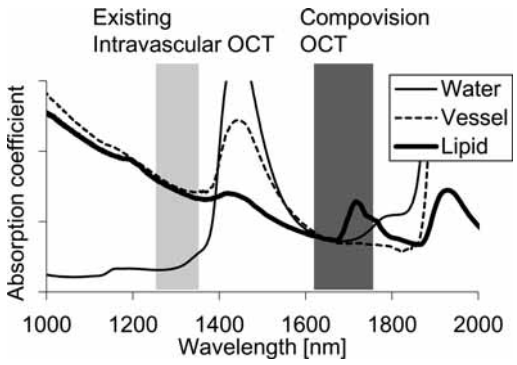

Fig. 2. Relationship between absorption spectra and OCT bands

3-2 Structure of CV-OCT

Figure 3 shows a photo of the CV-OCT system and **Fig. 4** shows the structural drawing. As in diagnostic systems using conventional coronary catheters, the light source, interferometer, spectroscopic line cameras, and control sys-

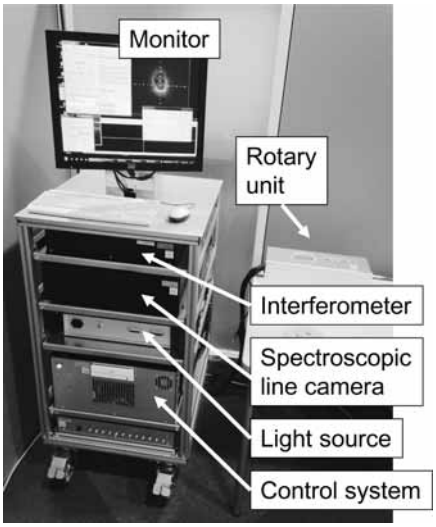

Fig. 3. Overview of CV-OCT

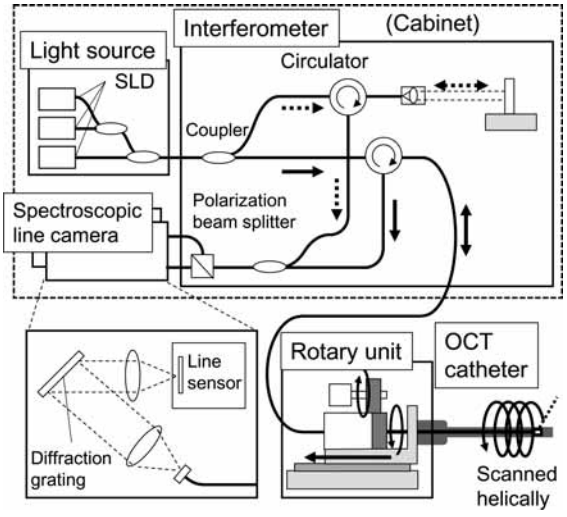

Fig. 4. Structural drawing of CV-OCT

tem are mounted on a movable cabinet, and a rotary unit for connecting the OCT catheter is placed outside the cabinet via a power cable and optical fiber cable.

The light source consists of three super-luminescent diodes (SLDs)[*6] customized to emit lights with different wavelengths at around 1.7 μm which are coupled to a single-mode coupler and the drive currents of the respective SLDs are adjusted so as to output flat spectra.

The interferometer consists of optical fibers and has the optical path for the reference light placed within the interferometer and path for the measurement light partly running outside the interferometer. After the measurement light and reference light are combined, the light is divided into two orthogonal components and received by separate spectroscopic line cameras to obtain constant interference regardless of the polarization state of the measurement light.

Each spectroscopic line camera consists of a lens, diffraction grating, and a line sensor that is sensitive to the 1.7-μm band wavelength and is designed to maximize the wavelength resolution that influences the image quality at the deeper part while ensuring the specified band.

The OCT catheter comprises an outer jacket consisting of a plastic tube and a rotatable inner body consisting of an optical fiber with a connector and sideway irradiation lens, and the lens is designed to focus light at a wavelength of 1.7 μm. Three-dimensional images of tubular structures such as blood vessels can be obtained by pulling and rotating the inner body of the OCT catheter with the rotary unit for helical scan.

3-3 Image processing with CV-OCT

Figure 5 shows the image processing flow of the CV-OCT. Cross-sectional images showing ordinary scattering distributions are obtained by continuously acquiring interference spectra while rotating the catheter, forming A-scan images from the interference spectra obtained with Fourier analysis, and placing the A-scan images in the lateral direction by the number of A-scans within one turn. Regarding the lipid distribution, a set of cross-sectional images are generated by dividing the interference spectra into several bands and applying Fourier analysis. Then these sub-band images are used for calculation with the weight of the absorption coefficient of the lipid at each band to obtain the distribution of the lipid content which is relative to the ordinary scattering distribution. The lipid distribution image can be obtained by laterally placing the distributions of the lipid content as an ordinary cross-sectional image.

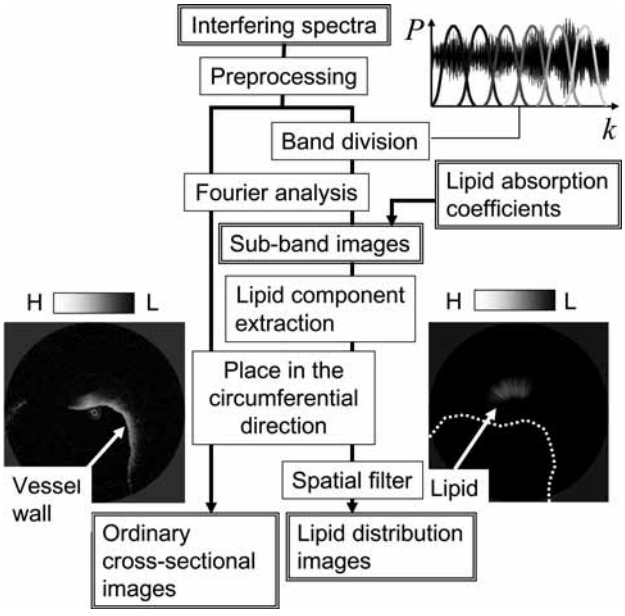

Fig. 5. Image processing flow of CV-OCT

3-4 Typical performance of CV-OCT

Figure 6 shows the spectral properties of the light source and the spectroscopic line camera. The light source has the output power of 19.6 mW and shows a flat spectrum with the 3-dB bandwidth of 128 nm including an absorption peak for lipid. On the other hand, the spectroscopic line camera covers the 156-nm bandwidth with the center wavelength of 1,690 nm.

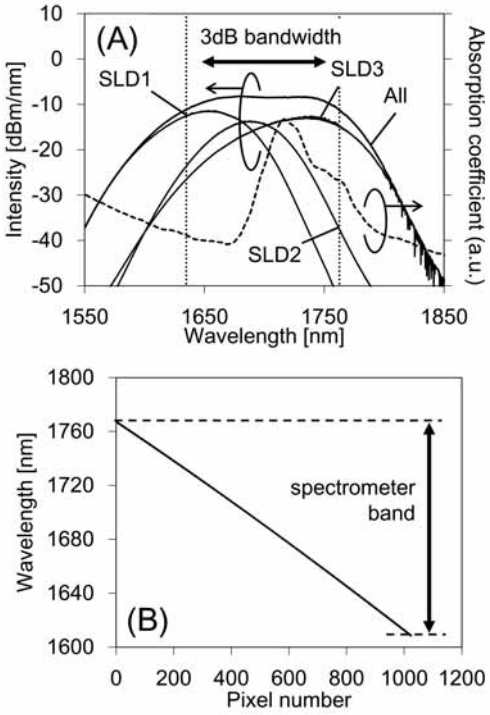

Fig. 6. Output spectra of the light source (A) and spectral properties of the spectroscopic line camera (B)

Table 1 shows the typical performance of the CV-OCT system[(5)]. The performance is obtained from the height, width and positional change of the reflection points of the A-scan image when a fiber reflector having a known reflectance is connected in place of the catheter and the optical path length difference of the interferometer is altered (**Fig. 7**). The sensitivity, expressed in dB, indicates the reciprocal of the minimum reflectance which can be de-

tected above the noise floor, and a sensitivity over 100 dB is generally required for imaging living tissue. When supercontinuum (SC) light that can emit similar broadband light was used instead of SLD, the speed of the A-scan remained at 1 kHz due to the strong influence of optical noise[4]. Thus the light source using SLD enables an improvement in the speed of 50 times. In intravascular OCT, the blood must be temporarily flushed using saline or the like during imaging. In addition, as images are taken with the heart constantly pulsating, an A-scan speed of at least tens of kilohertz is required to minimize the burden on the patient and acquire high-quality images. The performance of this CV-OCT is usable for intravascular diagnostics.

Table 1. Typical performance of CV-OCT

A-scan speed	47 kHz
Sensitivity (Max.)	104 dB
Observation range (in air)	4.6 mm
Axial resolution (in air)	18 μm
Roll-off distance (6 dB, in air)	2.9 mm
Number of A-scan images per frame	500
Rotational speed of the catheter	5,660 rpm

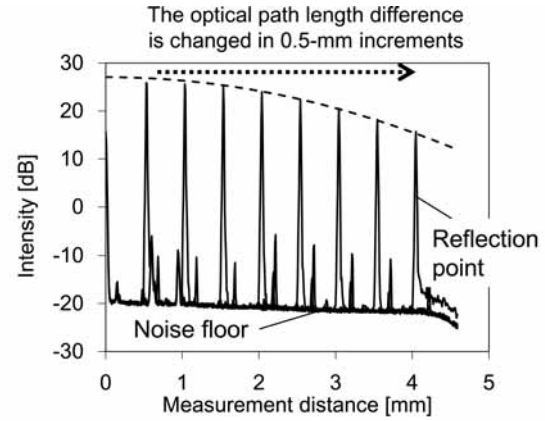

Fig. 7. A-scan image when the optical path length difference of the interferometer is changed

3-5 Demonstration of lipid determination

To verify the lipid determination ability, we prepared a blood vessel plaque model by inserting a nylon tube filled with lard as pseudo-plaque into a porcine coronary artery and scanned the inside of the vessel for 40 mm in the longitudinal direction using the OCT catheter (**Fig. 8**).

Figure 9 shows lateral and longitudinal cross-sectional views of the ordinary scattering distribution. Layer structures of the coronary artery and the shape of the nylon tube can be clearly observed. To visualize the lipid distribution image, an ROC curve[*7] related to determination between the blood vessel and lipid at a particular point were confirmed, and a determination ratio over 90% was shown with the optimum determination threshold (graph in **Fig. 10**). When lipid distributions at several points were superimposed using this determination threshold, a response to lard in the tubes was confirmed (images in **Fig. 10**). These results indicate the effectiveness of CV-OCT in composition diagnosis within blood vessels.

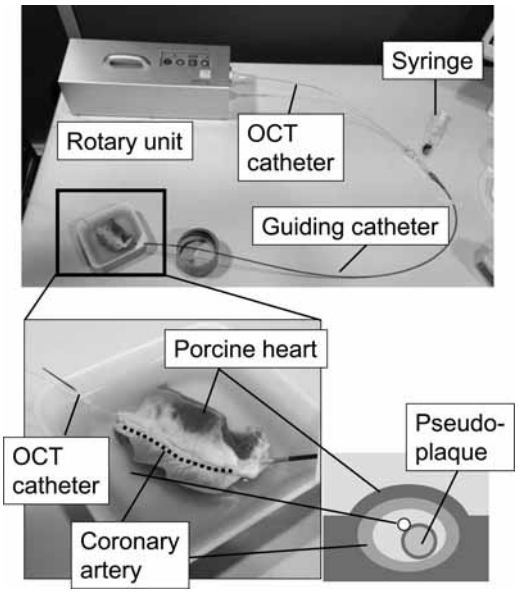

Fig. 8. OCT observation of blood vessel plaque model

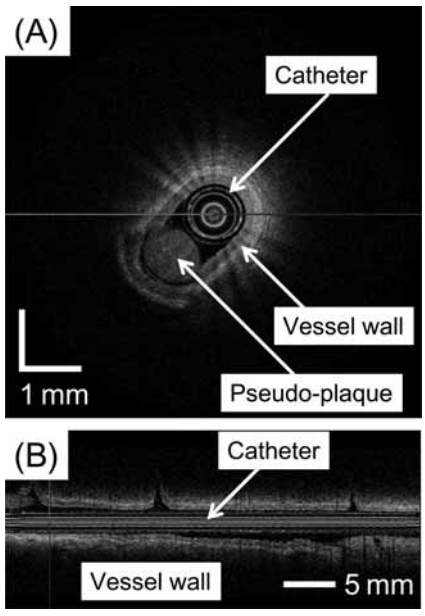

Fig. 9. Ordinary cross-sectional views of blood vessel plaque model in the lateral (A) and longitudinal (B) directions

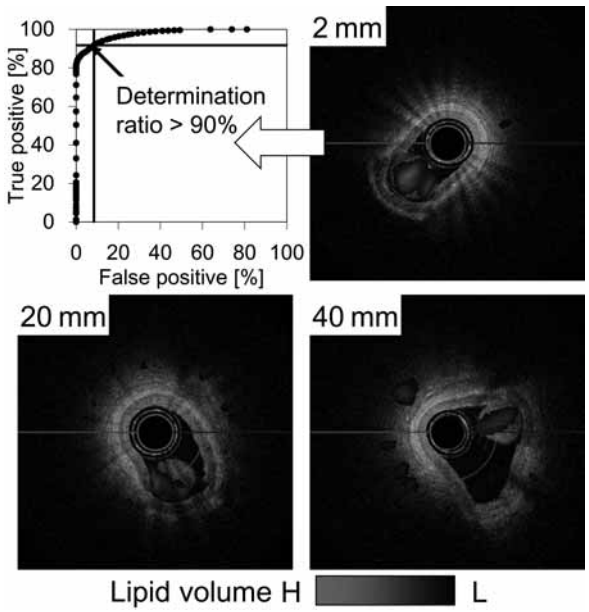

Fig. 10. Trend in lipid determination ratio (top left) and lipid distribution images at each point

4. Conclusion

We report on Compovision OCT in which the near-infrared analysis technique we developed is applied to intravascular OCT. We intend to enhance the image quality and the lipid determination ability and plan to conduct experimental observation of autopsy samples to simulate actual situations for practical application to intravascular diagnosis.

Technical Terms

*1 Catheter: A hollow tube used for medical applications. In intravascular diagnostics, two types of catheter are used: a guiding catheter inserted from the insertion port in the groin or on the wrist to a vascular lesion; and a catheter that is passed through the guiding catheter for diagnosis or treatment of the lesion.

*2 Plaque: A buildup in an artery due to arteriosclerosis. Plaque having a large lipid core in the center and covered by a thin fibrous cap is called vulnerable plaque. It is required to be detected on the earliest stage because it may rupture and is highly likely to cause acute myocardial infarction.

*3 Compovision: An analysis system we developed to detect composition distributions using near-infrared lights with wavelengths of 1,000 to 2,350 nm. It can examine the composition of pharmaceutical products and food in a non-destructive and non-invasive manner in real time.

*4 FD-OCT: There are two types of OCT: time-domain OCT (TD-OCT) which directly obtains cross-sectional images by constantly altering the optical path length difference; and Fourier-domain OCT (FD-OCT) which obtains cross-sectional images from spectra using Fourier analysis at a fixed optical path length difference. While cross-sectional images can readily be obtained with TD-OCT, a mechanism that alters the optical path length difference is needed and the sensitivity is lower than FD-OCT by 20 to 30 dB. FD-OCT is thus usually used for living tissue diagnosis for which high-speed imaging is required.

*5 Fourier analysis: A method of analysis that separates a waveform into sinusoidal waves with different frequencies.

*6 Super-luminescent diode: A light source that features the high-output power of a laser with the broad bandwidth of an LED. It is widely used for optical measurement or imaging in biotechnology and for medical uses.

*7 ROC: Acronym for receiver operating characteristics. In determining positives / negatives based on thresholds, the curve showing the relationship between the false-positive ratio (the ratio in which a negative is wrongly determined as a positive) and the true positive ratio (the ratio in which a positive is properly determined as a positive) on different thresholds is called an ROC curve. A determination with an ROC curve that is away from the diagonal line from the origin is considered favorable.

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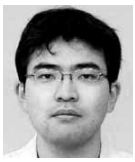

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